Lifespan increased with complex supplement

It's known that a number of natural and unnatural (drug) compounds increase lifespan in various laboratory animals, resveratrol, curcumin, and rapamycin for example. What happens if you feed a lab animal, in this case mice, a multi-ingredient supplement designed to increase lifespan? It works.

A Complex Dietary Supplement Extends Longevity of Mice. This study used both transgenic mice, designed to have high levels of growth hormone, and normal mice, and found that transgenic mice had their lifespans extended by 28%, and normal mice by 11%. For humans, that might equate to an extra ten years of life, and more importantly in my opinion, higher quality years.

Another paper with the same lead researcher, C. D. Rollo, found that the same supplement augments learning, brain mass, and mitochondrial activity in aging mice. This paper includes a list of the ingredients of the complex supplement, as follows:
The list is of the usual suspects in anti-aging research, notably including alpha lipoic acid, acetylcarnitine, and green tea extract. Notably missing is resveratrol. Note the inclusion of aspirin (acetylsalicylic acid). Generous doses of omega-3 oils, both cod liver and flax seed, are included.

The dose for a mouse may be translated into a human dose roughly by dividing by a factor of 12. (See here.) Also note that the above list is per 100 mice, so that factor must be taken into account.

Finally, the same supplement dramatically reduced the incidents of tumors and metastasis in tumor-prone mice.

You cannot get this level of supplementation through diet alone. Supplements are required.
Male Sexuality, Athletics, and Vitamin D

Why many people are deficient in vitamin D

Vitamin D has been in the news a lot over the past five years or so; it’s importance to human health was already recognized, but the realization has hit home that many people are deficient, and this has occurred because of man-made conditions. Let’s look at how male sexuality, athletics, and vitamin D fit together.

One condition, one that has taken place mainly since the Industrial revolution, is that most people no longer work outside in the sunshine, the main source of vitamin D, but indoors and away from the sun. The second condition is that we have all been told over the past several decades to avoid direct sunlight, for fear of skin cancer, so people have been deliberately avoiding sun exposure. As a result, many people are frankly deficient in vitamin D. Besides these reasons, depending on time of year and latitude, and it often be difficult to get enough sunshine to produce vitamin D.

How vitamin D affects male sexuality

New discoveries are being made constantly in vitamin D research, such as finding vitamin D receptors in tissues where they were heretofore unknown. Here’s a great example of finding vitamin D receptors, as well as vitamin D metabolizing enzymes, in a place where they were previously not known to occur: Vitamin D receptor and vitamin D metabolizing enzymes are expressed in the human male reproductive tract. An excerpt from the abstract:
The vitamin D receptor (VDR) is expressed in human testis, and vitamin D (VD) has been suggested to affect survival and function of mature spermatozoa.

On the basis of the marked expression of VDR and the VD metabolizing enzymes in human testis, ejaculatory tract and mature spermatozoa, we suggest that VD [vitamin D] is important for spermatogenesis and maturation of human spermatozoa.

Vitamin D is important in the male reproductive tract and for in male fertility. Indeed, Vitamin D is positively associated with sperm motility and increases intracellular calcium in human spermatozoa. And it’s been shown that vitamin D is necessary for male reproductive functions in rats.

**Vitamin D affects erectile function**

So we see that vitamin D affects male fertility. Does it also affect male sexual function? Some researchers believe it does. Noted vitamin D scientist William B. Grant collaborated on a review article that argues for the importance of D for erectile function: Does vitamin D deficiency contribute to erectile dysfunction? Quote: “We conclude that VDD [vitamin D deficiency] contributes to ED [erectile dysfunction]. This hypothesis should be tested through observational and intervention studies.” Vitamin D is closely and negatively related to diabetes and obesity, and these are in turn related to male potency.

A study was done on patients with erectile dysfunction, Vitamin D and Erectile Dysfunction. The scientists found that “a significant proportion of ED patients have a vitamin D deficiency and that this condition is more frequent in patients with the arteriogenic etiology. Low levels of vitamin D might increase the ED risk by promoting endothelial dysfunction. Men with ED should be analyzed for vitamin D levels…”

**Testosterone and vitamin D**

Vitamin D influences male sexuality through another channel as well, that of testosterone. There is a strong association between vitamin D and testosterone levels: Association of vitamin D status with serum androgen levels in men. This study concludes: “Androgen levels and 25(OH)D [vitamin D] levels are associated in men and reveal a concordant seasonal variation.” The seasonal variation reported indicates that sunshine, hence vitamin D, is an important influence on T levels. So testosterone is one route by which D may impact male sexual potency.

It also follows that if you are trying to build muscle mass, optimum vitamin D levels will be necessary to ensure proper levels of T.

**Ensuring proper vitamin D levels**

Don’t think that because you do outdoor sports or some similar activity that
you get enough vitamin D. In a recent study it was found that about one third of NCAA athletes in Southern California, the land of sunshine, had low vitamin D levels; athletes with dark skin and males were much more likely to be at risk of D deficiency. Quote: “studies examining muscle biopsies from patients with low vitamin D levels have demonstrated atrophic changes in type II muscle fibers, which are crucial to most athletes. Furthermore, insufficient 25(OH)D levels can result in secondary hyperparathyroidism, increased bone turnover, bone loss, and increased risk of low trauma fractures and muscle injuries. Despite this well-documented relationship between vitamin D and athletic performance, the prevalence of vitamin D deficiency in NCAA athletes has not been well studied.”

So, vitamin D is necessary for both strong muscles and strong bones.

Supplementation is one way to ensure optimal vitamin D levels. The Endocrine Society recommends screening of vitamin D levels for those at risk, and that 4,000 IU of vitamin D daily is a tolerable upper intake level for adults, “not to be exceeded without medical supervision.”

PS: Check out my Supplements Buying Guide for Men.

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**Book Promotion**

I’ve taken a cue from How to Beast and decided to promote my book on Kindle for one week by offering it at $2.99.

So if you haven’t already, you can buy the book, Best Supplements for Men’s Health, Strength, and Virility, at Amazon.

The book covers the reason you might need supplementation, such as fitness goals, aging, or just generally not eating right; specific supplements are covered, from whey and creatine to vitamin D, n-acetylcysteine, and aromatase inhibitors. And more.

The paperback version is coming soon, hopefully by next week.

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**Weightlifting, the most healthful exercise**
What’s healthier, aerobic exercise or weights?

I’ve long thought that weightlifting is the best, that is the most health-giving, exercise, but admittedly some of that is my own prejudice. On logical grounds, however, it would seem the best, since an exercise like running works the circulatory system and the legs, while weightlifting works everything. (This is leaving aside such forms of exercise as HIT, high intensity training, or Cross Fit, which have elements of both.)

But some recent studies show that weightlifting is indeed a very healthy thing to do.

**Weightlifting enhances the brain**

Study number one: *A single bout of resistance exercise can enhance episodic memory performance*. In this study, the researchers wanted to see whether resistance training (weightlifting) had a beneficial effect on memory. And it did: memory improved in the weightlifters by about 10%. This is similar to results from aerobic exercise, so weightlifting at least matches it in this category.

**Weightlifting prevents and treats sarcopenia**

Study number two relates to sarcopenia, the condition of loss of muscle mass that occurs mainly in older people. *Resistance Exercise for the Aging Adult:*
Clinical Implications and Prescription Guidelines. Quote: “Progressive resistance exercise should thus be encouraged among healthy adults to minimize degenerative muscular function associated with aging.” For comparison purposes, aerobic exercise will do very little to combat sarcopenia. It will do something, by helping to lower levels of inflammation and oxidative stress, two contributors to sarcopenia. But aerobic exercise will only help decrease the rate of muscle loss; it won’t build muscle. Resistance training will build muscle and strength, crucial for the health of older people. Sarcopenia is a serious condition that often leaves the elderly disabled and unable to function, headed for the nursing home or a hip fracture from a fall. And if you think that you’re not old enough to worry about this, think again: by age 40, adults start losing muscle mass at about 8% per decade, and this accelerates to about 15% per decade by age 70. (Link.) The best thing to do about sarcopenia is to stop it in the first place through weightlifting. (Protein has an important role in sarcopenia prevention too, but that’s outside the scope of this post.)

**Weightlifting lowers the death rate in cancer survivors**

Study number three, the capstone: The Effect of Resistance Exercise on All-Cause Mortality in Cancer Survivors. In this study, the researchers wanted to see whether weightlifting improved survival after cancer. I’ll let them have the floor:

“Physical activity in cancer survivors was not associated with a lower risk of all-cause mortality. In contrast, RE was associated with a 33% lower risk of all-cause mortality (95% CI, 0.45-0.99) after adjusting for potential confounders, including PA.

**Conclusion**

Individuals who participated in RE during cancer survival had a lower risk for all-cause mortality. The present findings provide preliminary evidence for benefits of RE during cancer survival. Future randomized controlled trials examining RE and its effect on lean body mass, muscular strength, and all-cause mortality in cancer survivors are warranted."

So, to spell it put, physical activity, that is, garden variety aerobic exercise, had NO effect on survival, but those who lifted weights had a 33% decrease in mortality from all causes.

So it’s no contest: weightlifting is the most healthful exercise you can do. It strengthens the brain, prevents sarcopenia, and lowers mortality in cancer survivors.

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**Depression: breaking the vicious cycle**

The positive feedback loop of depression
One problem with overcoming depression, whether it’s a longstanding one or just an episode of the blues, is that depression reinforces itself in a positive feedback loop. Depression causes inaction and lack of motivation, and these in turn reinforce the depression. You’re stuck.

For instance, it’s a well-replicated finding that exercise causes better mood and can be effective in depression. Yet depressed people generally do not want to exercise, because they’re in the grips of that positive feedback loop of demotivating depression.

**Stand, don’t sit**

So, how does one break that loop and take action that will help alleviate depression? Well, for one thing, small steps can matter. If you don’t feel up to exercising or getting moving, you can resolve to stand for long periods of time, hours, say. Sedentary behavior, which mainly comprises sitting, is “associated with significantly elevated risk of obesity and type 2 diabetes, whereas even light to moderate activity was associated with substantially lower risk.” Diabetes and obesity feature elevated levels of inflammation and oxidative stress, and in fact this holds true of depression, so there is a relationship. Standing can be looked at as a form of exercise, and one actually burns about 50% more calories while standing than while sitting. And just anecdotally, my own experience is that standing causes a significant mood elevation as well as a higher energy level.

Standing can also be put into action at work. If at home and not working, one can stand while reading a book, or stand in front of the computer using a standing desk. Or perhaps one can imitate the practice of certain Catholic priests, that of peripatetic reading. In any case, standing is easily enough done that there’s no excuse for sitting around, barring exceptional circumstances.

If Rumsfeld can handle it, I think I can handle it.

**Sleep deprivation for depression**

Another way to jump start your way out of the feedback loop of depression is sleep deprivation, or as it’s sometimes known in its kinder and gentler version, wake therapy. Sleep deprivation therapy for depression, despite it sounding counter-intuitive, is a longstanding and well-replicated finding in psychiatry. What’s more, it works rapidly and also for the majority of depressed people who do it. By rapidly I mean almost instantaneously: usually the depressed person has greatly decreased symptoms immediately upon awakening. The symptoms often return upon getting more sleep, but despite that, improvement in symptoms often lasts for weeks after only one bout of total or partial sleep deprivation. Scientists are unsure about the mechanism of improvement, but one idea is that it increases levels of brain-derived
neurotrophic factor (BDNF).

A practical method of sleep deprivation

Back when sleep deprivation as a treatment for depression got going, so-called total sleep deprivation was the rule. This is exactly what it sounds like: no sleep at all for one night. Later, it was found that partial sleep deprivation was almost or entirely as effective as total, especially when the deprived sleep is in the second half of the night. In partial sleep deprivation, one sets the alarm for four hours after one hits the sack, so that for example one will arise at 2:00 A.M. Then one does not sleep again until the following night. Advancing the sleep phase, that is, going to bed later each night, results in more lasting improvement.

It probably goes without saying, but if one does this, coffee will be quite useful. In any case, coffee is associated with less depression anyway, so it does double duty there.

Furthermore, bright light therapy added to sleep deprivation provides additional effectiveness. (And on its own, light therapy is as effective as antidepressant drugs.)

Conclusion

Exercise is an effective tool against depression, but exercise requires motivation, which is often lacking in depression. Some people need the small steps to get going in the fight against their depression. Standing, wake therapy, light therapy, and caffeine can all be useful, and the motivation required is small.

Iodine for infections

There’s quite a bit of information on the web about the internal use of iodine for urinary tract infections. See a list. Most or all of this info comes from naturopathic and holistic type folks, not from PubMed. I believe that in the old days, iodine in the form of tincture or Lugol’s was commonly used for urinary tract infections, but am unable to confirm this.

A couple days ago, my pet fish was obviously very ill, lying in the bottom of the bowl, hardly moving, refusing to eat. In fact, several times I had to tap the bowl because I thought he was dead. This went on for maybe five days, and I thought he was a goner for sure. Thinking that he had a bacterial infection, and also that his death was imminent and not knowing what else to do, I put one drop of Lugol’s iodine in his water. I was also concerned that that amount of iodine might be toxic to him. Guess what, the next day he was much better, and as of today it’s like he was never sick.
Last year, a friend of mine who has pet rats asked me what to do when her rat started bleeding. Seems that the most common cause for finding blood in a rat’s cage is a urinary tract infection. She of course didn’t want to spend a huge sum on a vet. Her rat was very sick, and I figured that an infection like that could easily kill him, especially if it got to his kidneys. So I told her to go to the drugstore and buy some tincture of iodine, and add a couple drops to his water bottle. Again, I wasn’t sure about dose and toxicity. (Note the skull and crossbones that a bottle of tincture of iodine displays.) Anyway, it worked like a charm; cured the little guy.

Not recommending this, but it might be useful information.

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**How magnesium deficiency and depression are linked**

A recent issue of *Nutritional Neuroscience* featured a review study of possible links between magnesium intake and depression: [Magnesium and depression: a systematic review](#).

The incidence of depression is increasing worldwide. Much is still unknown about the possible role of magnesium in depression prevention and treatment. Magnesium has an effect on biological and transduction pathways implicated in the pathophysiology of depression. The possible role of magnesium in depression prevention and treatment remains unclear.

Magnesium seems to be effective in the treatment of depression but data are scarce and incongruous. Disturbance in magnesium metabolism might be related to depression. Oral magnesium supplementation may prevent depression and might be used as an adjunctive therapy. However, more interventional and prospective studies are needed in order to further evaluate the benefits of magnesium intake and supplementation for depression.

So, there’s at least some evidence for the link between low magnesium and depression, which I discussed at more length in [my new book](#). Also, for a bit more speculative take that’s highly favorable to magnesium treatment of depression, see [Magnesium and major depression](#) (pdf).

How might magnesium work in depression? A group of scientists recently discovered that, in mice, [low magnesium intake was associated with changes in the levels of four key proteins in the brain](#).
There is evidence to suggest that low levels of magnesium (Mg) are associated with affective disorders, however, causality and central neurobiological mechanisms of this link are largely unproven. We have recently shown that mice fed a low Mg-containing diet (10% of daily requirement) display enhanced depression-like behavior sensitive to chronic antidepressant treatment. … Collectively, these findings provide first evidence of low magnesium-induced alteration in brain protein levels and biochemical pathways, contributing to central dysregulation in affective disorders.

It’s been estimated that up to 60% of Americans do not get the recommended amount of magnesium in the diet, which could go some way toward explaining rising levels of depression.

I've noted before that magnesium citrate is the best absorbed form of magnesium, so if you want to supplement, that form is the one to go with – not the common drugstore form, magnesium oxide, which is barely absorbed at all.

My new ebook: Best Supplements for Men’s Health, Strength, and Virility
My new ebook has dropped: *Best Supplements for Men’s Health, Strength, and Virility*. It’s a revised and expanded version of the previous one, which started with a blog post. And no, that’s not me on the cover, though I could see why many would be tempted to think that.

The book includes discussion of why you may very well need supplements, as well as discussion of whey protein, creatine, vitamin D, omega-3 fats, resveratrol, n-acetylcysteine, testosterone and aromatase inhibitors, and more. The last chapter is a brief summary of my views on diet, fasting, and exercise.

In these days of declining T levels, nutrient-poor food, older average age of the population of men, and sedentary life, it’s important to understand how various supplements can maintain and improve a man’s vitality, muscle mass, T levels, help prevent heart disease and cancer, and along with those promote a healthy mental state and good sex life. Although aging makes all of these challenges more difficult, the book is also written with men of all ages in mind.
Lifting Weights Increases Brain-Derived Neurotrophic Factor

Increased Strength Training Doubles BDNF Levels

Resistance training, i.e. weightlifting, increased levels of BDNF, or brain-derived neurotrophic factor. BDNF is a growth factor that causes growth of neurons and increased synaptic connections. Training augments resistance exercise induced elevation of circulating brain derived neurotrophic factor (BDNF). The change was transient, that is, resting BDNF levels did not change, but after several weeks of training, “the change in serum BDNF from rest to immediately post-exercise was 98% greater at post-intervention than at baseline.”

Our study is the first to demonstrate that resistance exercise induces a robust, yet transient, elevation of circulating BDNF and that progressive resistance training augments this response; perhaps demonstrating one mechanism through which exercise influences brain health.

Exercise is one of the most powerful anti-aging interventions you can do. Throw in some intermittent fasting and you’re golden.
Another study which was much touted at the time of publication found that exercise increases brain volume, specifically that of the hippocampus. Exercise training increases size of hippocampus and improves memory.

The hippocampus shrinks in late adulthood, leading to impaired memory and increased risk for dementia. Hippocampal and medial temporal lobe volumes are larger in higher-fit adults, and physical activity training increases hippocampal perfusion, but the extent to which aerobic exercise training can modify hippocampal volume in late adulthood remains unknown. Here we show, in a randomized controlled trial with 120 older adults, that aerobic exercise training increases the size of the anterior hippocampus, leading to improvements in spatial memory. Exercise training increased hippocampal volume by 2%, effectively reversing age-related loss in volume by 1 to 2 y. We also demonstrate that increased hippocampal volume is associated with greater serum levels of BDNF, a mediator of neurogenesis in the dentate gyrus. Hippocampal volume declined in the control group, but higher preintervention fitness partially attenuated the decline, suggesting that fitness protects against volume loss. These theoretically important findings indicate that aerobic exercise training is effective at reversing hippocampal volume loss in late adulthood, which is accompanied by improved memory function.

Note that both of these studies were trials and not mere association.

There have been some studies that showed that only endurance training had an effect on brain volume, but these studies refute that. Not only do your muscles grow when you lift weights, so does your brain.

Exercise is a potent way to retain brain volume with aging, or really at any age for that matter.

For more, see my book, Muscle Up. A few bucks can help you get healthy.
Curcumin as antidepressant.

Curcumin, the supplement derived from the spice turmeric, has all kinds of interesting properties, such as being anti-cancer and extending lifespan. Both of these together make perfect sense, since cancer is largely a disease of old age; anything that stops cancer will extend life, and vice versa.

Another interesting property is that it may be an effective antidepressant. This isn’t some wild, New Age stuff from people who just don’t like drugs, but is real and is being tested. Curcumin for the treatment of major depression: A randomised, double-blind, placebo controlled study. This study has as one of its co-authors the estimable Michael Maes, one of the preeminent names in biological psychiatry. (He is also the man who has generated many useful insights into the genesis and treatment of chronic fatigue syndrome.) From the abstract:

Background
Curcumin, the principal curcuminoid derived from the spice turmeric, influences several biological mechanisms associated with major depression, namely those associated with monoaminergic activity, immune-inflammatory and oxidative and nitrosative stress pathways, hypothalamus-pituitary-adrenal (HPA) axis activity and neuroprogression. We hypothesised that curcumin would be effective for the treatment of depressive symptoms in individuals with major depressive disorder.

Methods
In a randomised, double-blind, placebo-controlled study, 56
individuals with major depressive disorder were treated with curcumin (500 mg twice daily) or placebo for 8 weeks. The primary measure was the Inventory of Depressive Symptomatology self-rated version (IDS-SR30). Secondary outcomes included IDS-SR30 factor scores and the Spielberger State-Trait Anxiety Inventory (STAI).

Results
From baseline to week 4, both curcumin and placebo were associated with improvements in IDS-SR30 total score and most secondary outcome measures. From weeks 4 to 8, curcumin was significantly more effective than placebo in improving several mood-related symptoms...

Conclusions
Partial support is provided for the antidepressant effects of curcumin in people with major depressive disorder, evidenced by benefits occurring 4 to 8 weeks after treatment.

Limitations
Investigations with larger sample sizes, over extended treatment periods, and with varying curcumin dosages are required.

The dose strikes me as being not all that much. This article suggests that doses up to several grams a day are safe.

Curcumin may work in this way by increasing, or preventing the decrease of, levels of BDNF, brain-derived neurotrophic factor.

Three simple and effective ways to slow aging and increase lifespan

A recent study found that raising levels of the cell signaling molecule AMPK increased lifespan in fruit flies by 30%. (Cell Reports, PDF, press release.) AMPK did this by increasing activity of autophagy, which is the regulated process of cellular degradation, essentially removing junk molecules and organelles from the cells.

So by increasing AMPK and therefore autophagy, one has a good shot at retarding aging and increasing lifespan and health. There are a number of ways to do this, and they consist of all the usual suspects.

1. Intermittent fasting: “It is then the question of what the optimal strategy would be to improve healthy aging by enhancing autophagy without deleterious side effects. Intermittent fasting, for instance by alternating days of starvation with days of ad libidum feeding, can increase the life
span of rodents as much as chronic caloric restriction without a concomitant major decrease in body mass—a measure that may avoid the negative effects of caloric restriction on bone density and consequent pathological fractures.”

Calorie restriction, while effective at increasing longevity, results in decreased muscle and bone mass, besides the fact that permanently reducing calories by ~30% is very difficult, and results in low body temperatures and low libido. Intermittent fasting appears to offer all the benefits of calorie restriction with few of the drawbacks. A simple way to put intermittent fasting into effect is to eat only during an 8-hour feeding window daily, say 11 A.M. to 7 P.M. During the 16-hour fasting period, nothing is taken except perhaps coffee, tea, and water—these should be taken, as they make fasting much easier by decreasing hunger. The beauty of the 16-hour fasting period is that one is asleep for much of that time, and it involves extending a natural 12 hour fast by just a few hours.

2. Curcumin induces autophagy, as does resveratrol. Both are inexpensive OTC supplements that appear to have little downside. Autophagy knockout cells do not show increased stress resistance with curcumin or resveratrol, which shows that autophagy is the mechanism through which these compounds work.

3. Exercise induces autophagy, and in fact looks to be required to get the beneficial effects from exercise. How much exercise is a good question, but it seems that an intense exercise session of any kind should do it.
Drinking alcohol is healthy – or is it?

The evidence for alcohol and health

At Pacific Standard, a doctor, Stanton Peele, writes, The Truth We Won’t Admit: Drinking Is Healthy. He cites a number of studies that show greatly decreased mortality is associated with drinking alcohol. He even goes beyond what articles of this kind usually say, and that is that you can drink quite a lot and still get health benefits. Most such studies and articles come with the caveat that more than one or two drinks a day for a man, or just one for a woman, reduces health benefits, but Peele shows that even a man who has four drinks a day still has a lower mortality than a complete abstainer.

He also shows that another caveat is not relevant. This one is that the group of teetotalers will include both those who are too ill to drink as well as former alcoholics, and since they are likely to die younger, this skews the mortality statistics in favor of drinkers. But a study of only healthy people that controlled for things like smoking and BMI still found that drinkers had an advantage.

Peele also asserts that the legacy of the temperance movement and America’s love-hate attitude to alcohol prevents doctors and health authorities from recommending drinking alcohol as a means to better health, and I think he may have a point.

Drinking is not the causative factor of longer life

There’s only one problem: all the studies he cites are associational only. In other words, people who drink alcohol live longer, but it is far from being proven that alcohol is the cause of longer life. What is needed is a randomized controlled trial in which one group is counseled to drink, the other to abstain, and then see what happens. As far as I can tell, such a study has not been done.

Higher intelligence is robustly associated with better health

The biggest confounder in these studies is that intelligent people drink more alcohol, and IQ is robustly associated with longer life and better health. As the association between drinking and intelligence is often thought counter-intuitive by many people, I reproduce one of the graphs from Kanazawa:
So, the more intelligent people are, the longer they live, and the more they drink, but alcohol seems quite unlikely, in my view, to be the cause of longer life.

Where does that leave us?

I think that one thing we can say about alcohol is that it’s not all bad, it doesn’t harm health if drinking is moderate, at least as far as we can tell. But drinking for one’s health probably won’t work, and unfortunately IQ is hardly malleable at all, so nothing one can do there.

Bottom line: moderate drinking probably won’t kill you, but it probably won’t help much either. Cheers!
What is whey, and what’s it good for?

Whey is the fraction of protein from milk that remains liquid when milk is curdled. The curdled portion mostly represents casein – which has its uses, but that’s for another time. Hence whey has traditionally been a byproduct of cheese making, since only the curds are useful for that.

Whey is especially useful in bodybuilding and weightlifting, for a number of reasons. One is that it has a high content of branched-chain amino acids.
(BCAAs), and these are important as signals that tell muscle to grow. It’s also high in essential amino acids (EAAs), which are the kind the body cannot make for itself. Whey is about 25% BCAAs, and about 50% EAAs. Along the same lines, whey is a “fast” protein, so a whey shake delivers an abundant amount of the right kind of amino acids quickly into the bloodstream, and this is a crucial determinant of the amount of muscle protein synthesis one gets from a workout. Even absent a workout, a dose of protein can help overcome sarcopenia (muscle wasting) in older people, which I wrote about here.

**Whey can help cure chronic illnesses**

There’s another aspect to whey, which is that properly made, it contains a number of biologically active peptides, that is, short-chain strings of amino acids. Among these are alpha-lactalbumin, beta-lactoglobulin, and immunoglobulins. The caveat here is “properly made”, since ordinary processing destroys these peptides, breaking them down into their constituent amino acids.

These biologically active peptides can be useful in other contexts besides weightlifting. They promote higher glutathione levels and a better immune response. As such, whey may be useful in cancer prevention. There’s even been a clinical trial on patients with metastatic breast cancer. There’s some evidence that this type of whey can improve cognition. They also may increase endurance performance.

**The best whey options**

One catch here is that the specific kind of whey used in many of the studies linked above is called Immunocal, and it’s quite expensive at over $130 for a pack of 30 10 gram packets. A serious weightlifter would burn through that in no time.

Another catch is that most whey of the kind sold in nutrition stores and the like is not undenatured. It’s manufactured using whey left from cheese manufacturing and by acid processing, which means that no biologically active peptides remain. This kind will definitely still build muscle, but if you want all the health benefits of whey, you need to look elsewhere.

So the kind I like and use myself is a cold-processed, undenatured whey made by NutraBio. It’s got the biologically active peptides, but at around the same price as garden-variety whey. Be sure to get the concentrate, or the isolate, but not the hydrolyzed version, as this will not have those peptides.

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**Can you increase your lean mass**
through diet alone?

What's the relation of dietary protein to lean mass?

How does dietary protein relate to lean mass – mainly muscle – in the absence of resistance training or any other form of exercise? Can you increase muscle just through a change in diet? Some researchers decided to find out:

*Increased Fat-Free Body Mass and No Adverse Effects on Blood Lipid Concentrations 4 Weeks after Additional Meat Consumption in Comparison with an Exclusion of Meat in the Diet of Young Healthy Women*. In this study, the researchers divided a number of young women into two groups: one with additional meat in the diet, the other with no meat at all. The study lasted four weeks. In that time, the additional meat group gained .7 kg – about 1.5 lbs. – of lean mass, and the no meat group lost about the same in lean mass.

The meat group ate an additional 270 calories a day but gained no fat. They also ate about 2.25 grams of protein per kg bodyweight, which is a large amount, well into bodybuilders’ territory. The no-meat group consumed about 1.15 g/kg protein daily. So all of the additional calories of the meat group were either burned or turned into muscle, or possibly other lean mass, such as bone.

The current opinion of exercise physiology is that about 1.8 grams of protein per kilogram of bodyweight maxes out the amount of muscle protein synthesis possible, anything above that being superfluous and burned off. The meat group in this study was well above that, but we don’t know whether they didn’t need that much, 1.8 g/kg being adequate, or whether they used all that excess protein.

Can even more protein be beneficial?

But is there any evidence that more protein than 1.8 g/kg can be beneficial? In fact there is, if one is trying to lose weight by restricting calories. In *Evidence-based recommendations for natural bodybuilding contest preparation: nutrition and supplementation*, the authors state that bodybuilders getting ready for competition by restricting calories really need to up the protein content of their diet to avoid losing muscle. It appears that well over 2 g/kg a day are necessary in this particular circumstance. In this case, the higher protein didn’t put on muscle, but prevented bodybuilders who were trying to get shredded from losing muscle.

If you’re dieting to lose weight, a much higher protein intake appears to be beneficial, since it will help preserve muscle, which you do not want to lose.

The gross inadequacy of U.S. government guidelines for protein

I found one aspect of the first-linked study on young women rather ominous, and that is that on an intake of 1.15 g/kg a day of protein, they lost lean mass. Yet at the same time the RDA, Recommended Dietary Allowance, for
protein is only 0.8 grams per kilogram bodyweight, or about 56 grams a day for a 70 kg man. If young women lost lean mass on a diet that provided more protein than that, obviously something is wrong. What’s wrong is the RDA for protein, which ought to be much higher. In *The underappreciated role of muscle in health and disease*, the author suggests that up to 1.8 g/kg bodyweight would be much healthier, as it’s been shown that the RDA cannot maintain lean mass in older people. Or probably younger, as we’ve just seen.

**Bottom line**

If you already eat a diet relatively high in protein, featuring some animal protein at each meal, you may not be able to increase lean mass much by eating more protein. On the other hand, if you follow U.S. guidelines, you should stop that, increase your protein, gain some lean mass, and become healthier, whether you are a strength athlete or not.

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**Glucosamine extends lifespan, mimics low-carb diet**

Awhile back I posted on the fact that the OTC supplement glucosamine extends lifespan in both *C. elegans* and in mice. The mechanism resembles that of a low-carb diet.(1) The study’s main author, Michael Ristow, who is one of the leading lights in aging research, started taking glucosamine after this research. From the abstract:

> d-Glucosamine (GlcN) is a freely available and commonly used dietary supplement potentially promoting cartilage health in humans, which also acts as an inhibitor of glycolysis. Here we show that GlcN, independent of the hexosamine pathway, extends *Caenorhabditis elegans* life span by impairing glucose metabolism that activates AMP-activated protein kinase (AMPK/AAK-2) and increases mitochondrial biogenesis. Consistent with the concept of mitohormesis, GlcN promotes increased formation of mitochondrial reactive oxygen species (ROS) culminating in increased expression
of the nematodal amino acid-transporter 1 (aat-1) gene. Ameliorating mitochondrial ROS formation or impairment of aat-1-expression abolishes GlcN-mediated life span extension in an NRF2/SKN-1-dependent fashion. Unlike other calorie restriction mimetics, such as 2-deoxyglucose, GlcN extends life span of ageing C57BL/6 mice, which show an induction of mitochondrial biogenesis, lowered blood glucose levels, enhanced expression of several murine amino-acid transporters, as well as increased amino-acid catabolism. Taken together, we provide evidence that GlcN extends life span in evolutionary distinct species by mimicking a low-carbohydrate diet.

Impaired glucose metabolism means that the organism must upgrade its fat-burning machinery, and it does so by increasing the numbers of mitochondria.

Another study determined that there was an association in humans between glucosamine consumption and lower mortality rates.

Current (baseline) glucosamine and chondroitin use were associated with a decreased risk of total mortality compared to never use. The adjusted hazard ratio (HR) associated with current use of glucosamine (with or without chondroitin) was 0.82 (95% CI 0.75–0.90) and 0.86 (95% CI 0.78–0.96) for chondroitin (included in two-thirds of glucosamine supplements). Current use of glucosamine was associated with a significant decreased risk of death from cancer (HR 0.87 95% CI 0.76–0.98) and with a large risk reduction for death from respiratory diseases (HR 0.59 95% CI 0.41–0.83).

So about a 20% decrease in mortality rates with glucosamine, and around 40% decrease in death from respiratory diseases. This looks to be solid data, since many risk factors were adjusted for, such as BMI, smoking, etc., and there were more than 77,000 participants.

What I would like to know is whether glucosamine extends lifespan even in the presence of a low-carb diet, or whether it would be superfluous in that case.

This also tells us that a low-carb diet is a healthy one, and probably extends lifespan on its own.

What happens when you see the doctor

You’ve got some kind of physical or mental complaint and go to your doctor. What happens?

He’ll very likely prescribe a drug, one that has side effects and in many
cases could be worse than the illness. Sure, if you have an infection, you need an antibiotic. If you have a broken bone, you need painkillers (and more). Many conditions exist for which modern medicine literally saves lives.

What about if you have high blood pressure? This is a condition which lifestyle factors are important. But does any doctor prescribe diet? No, not a one, or at least as statistically close to zero as you could want. And even if they did, they don’t know what to prescribe. In many cases, they’re just as out of shape as their patients. No, you’ll get a pill, which has serious side effects.

In doctors’ defense, precious few of their patients will do anything to help themselves beyond popping a pill. So even were they so inclined, they don’t discuss lifestyle factors – diet, exercise, sleep – or OTC supplements.

What if you’re depressed? Medication can be of value, but these do have real and serious side effects, including possible long-term effects on the brain or perhaps a little suicidal ideation. However, they’re a doctor’s first resort. Exercise, magnesium, light therapy, n-acetylcysteine, even sleep deprivation therapy, all these can combat depression, and doctors are either ignorant of them or won’t bother telling patients about them. Mostly the former, I think.

What if you have fatigue? This is possibly the number one symptom that patients tell doctors about. If the doctor discovers that his patient isn’t sleeping well, he’ll prescribe a sleeping pill, paying no attention to the coffee the patient drinks all afternoon that prevents him from sleeping. Again: diet, exercise, OTC supplements? No.

Feeling a little fuzzy in the head? Forget all the sugar you ingest and your lack of sleep. What you need is speed.
Overcoming anabolic resistance for the older man and the hardgainer

What is anabolic resistance?

Anabolic resistance is the phenomenon in which muscle does not respond to stimulus with normal muscle protein synthesis, but rather a reduced response. The stimuli that would elicit such a response are resistance training, as the academics call it, and ingestion of protein. In young, healthy people, these stimuli cause increased muscle synthesis, and over the longer term this means bigger muscles, as they adapt to continued stimulus.
Sarcopenia and the “hard gainer”

In sarcopenia, that is muscle wasting, which is most often seen in older people, basal muscle anabolism and catabolism can be normal, but the muscle fails to respond properly to stimulus, namely resistance training and protein consumption.

In younger men, we find the phenomenon of the so-called “hard gainer”, the guy who lifts and lifts and eats and eats, but can’t seem to put on much muscle, or at least finds it much more difficult than others to do so.

The cause of anabolic resistance

Anabolic resistance has actually been studied a fair amount because it’s a common condition in older people that leads to sarcopenia. Since sarcopenia often leads to disability, the inability to care for oneself (nursing homes) and ultimately death (from falls leading to hip fractures and the like), anabolic resistance is actually a major public health problem.

Researchers often focus on ways to fix it, but as to the cause, they are often reduced to saying that it’s just “age”. Sure, we know detailed cellular mechanisms of resistance, but why age causes these is another story.

However, I’ve come to the rescue, since I know what causes anabolic resistance. In a nutshell, inflammation, which increases greatly with age. Inflammation is also a cause of insulin resistance, also more common with age, and the two are related. It follows that with less inflammation and greater insulin sensitivity, anabolic resistance will diminish.

A large clue to how all this works is the fact that omega-3 fatty acids from fish oil are anabolic. For example, omega-3 polyunsaturated fatty acids augment the muscle protein anabolic response to hyperinsulinaemia-hyperaminoacidaemia in healthy young and middle-aged men and women. In this study, fish oil caused a ~30% increase in muscle protein synthesis, and a ~50% increase in mTOR phosphorylation.

Even better results were seen in the elderly: Dietary omega-3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: a randomized controlled trial.

Fish oil can also help treat a condition that’s similar to sarcopenia, cachexia: Eicosapentaenoic acid (EPA, an omega-3 fatty acid from fish oils) for the treatment of cancer cachexia.

How does fish oil decrease anabolic resistance?

Fish oil decreases anabolic resistance probably by two different means: it decreases inflammation, and restores normal fluidity in cell membranes, allowing receptors to work properly. Fish oil has clinically important anti-inflammatory effects.

How to overcome anabolic resistance
There are several ways that anabolic resistance may be overcome.

1. **Fish oil**: by decreasing inflammation and increasing insulin and other receptor sensitivity.
2. **Increased protein consumption**: In younger people, 20 grams of protein in one meal may be enough to promote maximum protein synthesis. Older people may need more. In one study, *older men undergoing resistance training had better muscle protein synthesis when they ingested 40 grams of whey protein as opposed to 20.*
3. **Exercise itself reduces anabolic resistance.**
4. **“Faster” protein**: the protein in meat, eggs, and the like digests slowly, and amino acids in the bloodstream therefore do not rise to as high a level as they do with a protein that digests faster, such as whey. The level of amino acids in the blood is a crucial determinant of anabolism. Therefore, taking a fast protein such as whey, whether with a workout or without it, will cause greater anabolism, other things being equal, such as quantity.
5. **BCAAs and leucine**: BCAAs, particularly leucine, crucially determine the amount of muscle protein synthesis. So ingesting protein high in BCAAs / leucine will cause greater anabolism. Whey has the highest fraction of BCAAs of any protein.
6. **In older people, resistance training**: It appears that sarcopenia may arise from a combination of inflammation (“inflammaging”) or just disuse. Older people typically have good responses to resistance training, even into their 90s.

**Don’t let age be an excuse**

There you have it. It is not “age” that causes anabolic resistance, but various metabolic derangements that accompany it. If you’re older, or you’re a hard gainer, you can use some of these methods I outlined to overcome anabolic resistance.

P.S.: I was asked what type of whey I like, and the answer is NutraBio, which is cold-processed and undenatured. Best one available, IMO.

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**N-acetylcysteine increases endurance performance**

**Production of free radicals is a determinant of performance and fatigue**

One of the crucial determinants of fatigue is the production of radical oxygen species (ROS, also known as free radicals) and internal antioxidant status, the latter mainly consisting of total, reduced, and oxidized glutathione. Glutathione is a tripeptide consisting of three amino acids, and the rate-limiting amino acid – the bottleneck to production – is cysteine. So, if more cysteine is provided, more glutathione will be produced. N-
acetylcysteine, the cheap over-the-counter supplement, provides cysteine, which cannot be taken in its native form due to high potential for oxidation.

When one performs any kind of intense or prolonged exercise, a large quantity of ROS is generated, and it’s mainly glutathione that mops them up and keeps the body from entering a condition of oxidative stress. Glutathione can be thought of as an exercise buffer. But when it is depleted, the body is overwhelmed with ROS, and fatigue ensues.

**N-acetylcysteine increases glutathione**

The main function of n-acetylcysteine (NAC) is to increase glutathione levels. When ingested, it is rapidly taken up by cells, de-acetylated to cysteine, and then used in glutathione production. Since NAC does this, and since glutathione is a determinant of fatigue, it follows that NAC should increase exercise performance.

**N-acetylcysteine significantly increases endurance and time to fatigue**

Lo and behold, NAC does work this way: N-acetylcysteine enhances muscle cysteine and glutathione availability and attenuates fatigue during prolonged exercise in endurance-trained individuals. In this study, trained cyclists who received NAC increased their endurance performance, that is, time to fatigue, by a remarkable 26%. NB: the cyclists received a lot of NAC, in fact a constant IV infusion.

Another study that used a special type of whey as a cysteine donor found increased peak power and 30-second work capacity: Effect of supplementation with a cysteine donor on muscular performance.

And in a study on rats, those that had a glutathione deficiency had a 50% reduced endurance performance.

**Fatigue of any kind is related to glutathione levels**

In my book on chronic fatigue, I discuss at some length the relation between chronic fatigue and glutathione levels, which is critically important for those suffering from long-term fatigue from any cause. NAC can be of help in that condition as well. So we see that fatigue, whether from unknown cause, illness, bad nutrition, or prolonged exercise is related to glutathione. This is not the sole determinant of fatigue, but an important one.